

Adenosine deaminase deficiency

Description

Adenosine deaminase (ADA) deficiency is an inherited disorder that damages the immune system and causes severe combined immunodeficiency (SCID). People with SCID lack virtually all immune protection from bacteria, viruses, and fungi. They are prone to repeated and persistent infections that can be very serious or life-threatening. These infections are often caused by "opportunistic" organisms that ordinarily do not cause illness in people with a normal immune system.

The main symptoms of ADA deficiency are pneumonia, chronic diarrhea, and widespread skin rashes. Affected children also grow much more slowly than healthy children and some have developmental delay.

Most individuals with ADA deficiency are diagnosed with SCID in the first 6 months of life. Without treatment, these babies usually do not survive past age 2. In about 10 percent to 15 percent of cases, onset of immune deficiency is delayed to between 6 and 24 months of age (delayed onset) or even until adulthood (late onset). Immune deficiency in these later-onset cases tends to be less severe, causing primarily recurrent upper respiratory and ear infections. Over time, affected individuals may develop chronic lung damage, malnutrition, and other health problems.

Frequency

Adenosine deaminase deficiency is very rare and is estimated to occur in approximately 1 in 200,000 to 1,000,000 newborns worldwide. This disorder is responsible for approximately 15 percent of SCID cases.

Causes

Adenosine deaminase deficiency is caused by mutations in the *ADA* gene. This gene provides instructions for producing the enzyme adenosine deaminase. This enzyme is found throughout the body but is most active in specialized white blood cells called lymphocytes. These cells protect the body against potentially harmful invaders, such as bacteria and viruses, by making immune proteins called antibodies or by directly attacking infected cells. Lymphocytes are produced in specialized lymphoid tissues including the thymus, which is a gland located behind the breastbone, and lymph nodes, which are found throughout the body. Lymphocytes in the blood and in lymphoid tissues

make up the immune system.

The function of the adenosine deaminase enzyme is to eliminate a molecule called deoxyadenosine, which is generated when DNA is broken down. Adenosine deaminase converts deoxyadenosine, which can be toxic to lymphocytes, to another molecule called deoxyinosine that is not harmful. Mutations in the *ADA* gene reduce or eliminate the activity of adenosine deaminase and allow the buildup of deoxyadenosine to levels that are toxic to lymphocytes.

Immature lymphocytes in the thymus are particularly vulnerable to a toxic buildup of deoxyadenosine. These cells die before they can mature to help fight infection. The number of lymphocytes in other lymphoid tissues is also greatly reduced. The loss of infection-fighting cells results in the signs and symptoms of SCID.

[Learn more about the gene associated with Adenosine deaminase deficiency](#)

- ADA

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- ADA deficiency
- ADA-SCID
- Adenosine deaminase deficient severe combined immunodeficiency
- SCID due to ADA deficiency
- Severe combined immunodeficiency due to ADA deficiency
- Severe combined immunodeficiency, autosomal recessive, T cell-negative, B cell-negative, NK cell-negative, due to adenosine deaminase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Severe combined immunodeficiency due to ADA deficiency (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863236/>)

Genetic and Rare Diseases Information Center

- Adenosine deaminase deficiency (<https://rarediseases.info.nih.gov/diseases/5748/adenosine-deaminase-deficiency>)

Patient Support and Advocacy Resources

- Disease InfoSearch (<https://www.diseaseinfosearch.org/>)
- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (<https://clinicaltrials.gov/ct2/results?cond=%22Severe+Combined+Immunodeficiency%22+OR+%22adenosine+deaminase+deficiency%22>)

Catalog of Genes and Diseases from OMIM

- SEVERE COMBINED IMMUNODEFICIENCY, AUTOSOMAL RECESSIVE, T CELL-NEGATIVE, B CELL-NEGATIVE, NK CELL-NEGATIVE, DUE TO ADENOSINE DEAMINASE DEFICIENCY (<https://omim.org/entry/102700>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28Severe+Combined+Immunodeficiency%5BMAJR%5D%29+AND+%28adenosine+deaminase+deficiency%5BTIAB%5D%29+OR+%28ada-scid%5BTIAB%5D%29+OR+%28adenosine+deaminase+deficient+severe+combined+immunodeficiency%5BTIAB%5D%29+OR+%28ada+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>)

References

- Blackburn MR, Thompson LF. Adenosine deaminase deficiency: unanticipated benefits from the study of a rare immunodeficiency. *J Immunol.* 2012 Feb;188(3):933-5. doi: 10.4049/jimmunol.1103519. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22262755>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3341658/>)
- Buckley RH. Molecular defects in human severe combined immunodeficiency and approaches to immune reconstitution. *Annu Rev Immunol.* 2004;22:625-55. doi: 10.1146/annurev.immunol.22.012703.104614. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15032591>)
- Hershfield MS. Genotype is an important determinant of phenotype in adenosine deaminase deficiency. *Curr Opin Immunol.* 2003 Oct;15(5):571-7. doi:10.1016/s0952-7915(03)00104-3. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/14499267>)

- Hershfield MS. New insights into adenosine-receptor-mediated immunosuppression and the role of adenosine in causing the immunodeficiency associated with adenosine deaminase deficiency. *Eur J Immunol.* 2005 Jan;35(1):25-30. doi:10.1002/eji.200425738. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15580654>)
- Nofech-Mozes Y, Blaser SI, Kobayashi J, Grunebaum E, Roifman CM. Neurologic abnormalities in patients with adenosine deaminase deficiency. *Pediatr Neurol.* 2007 Sep;37(3):218-21. doi: 10.1016/j.pediatrneurol.2007.03.011. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17765813>)
- Nyhan WL. Disorders of purine and pyrimidine metabolism. *Mol Genet Metab.* 2005 Sep-Oct;86(1-2):25-33. doi: 10.1016/j.ymgme.2005.07.027. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16176880>)

Last updated July 1, 2013